

**DETAILED ACTION**

Applicant's response to restriction requirement and amendment of 3/14/11 are entered.

Claims 58-60 are newly presented.

Claims 46-57 are amended.

Claims 46-60 are presently pending.

***Election/Restrictions***

Claims 54-57 are withdrawn from further consideration pursuant to 37 CFR 1.142(b) as being drawn to a nonelected inventions and Claims 51, 52 and 60 are withdrawn as being drawn to nonelected species, there being no allowable generic or linking claim. Election was made **without** traverse in the reply filed on 3/14/11.

Claims 46-50, 53, 58 and 59 are presently considered with respect to the elected species of Chemically modified RNA as the oligonucleotide, RNAi as the nucleic acid, and DMPC/MoChol/DGSucc/Chol at 40:10:10:40 as the composition.

***Information Disclosure Statement***

It is noted that the german references cited are not considered for failure to provide a copy.

***Drawings***

The drawings are objected to.

The panels are difficult to interpret, as to which is a micrograph or microscopic image, and what is shown. To wit, the left panel is almost completely black with a few dots, and the image on the right is a bunch of small squiggly-lines. The interpretation is difficult from such poor quality images. Applicant should submit the photographs or better quality photocopies.

New corrected drawings in compliance with 37 CFR 1.121(d) are required in this application for the reasons above. Applicant is advised to employ the services of a competent patent draftsperson outside the Office, as the U.S. Patent and Trademark Office no longer prepares new drawings. The corrected drawings are required in reply to the Office action to avoid abandonment of the application. The requirement for corrected drawings will not be held in abeyance.

### ***Specification***

The specification is objected-to.

The brief description of the drawings indicates that Figure 3 is listed as a phase contrast micrograph and fluorescence-microscopic image for cell localization, but does not indicate which is which, from the two panels which make up Figure 3. Such obfuscates understanding.

### ***Claim Rejections - 35 USC § 112***

The following is a quotation of the second paragraph of 35 U.S.C. 112:

The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claims 53 and 58 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claim 53 recites “a molar composition selected from …” then lists several ratios, e.g., “40:10:10:40”, but fails to identify that this “molar composition” what basis this ratio is given within. Is this a mole percent? Or is it absolute numbers of mols (indicating non-enablement), is it nanomolar ratios? Such is exacerbated by the ability to claim mol % with respect to the other claims (e.g., Claims 46 and 58). Hence, the Artisan would not know what is being claimed.

Claim 58 recites “said mixtures” in Claim 46. The claim lacks proper antecedent basis. However, there are no generic “mixtures” in Claim 46, only “mixtures of cationic and anionic lipids”. Hence, the Artisan would not know if Applicant is claiming the mixture of all components, or any particular mixture of the required components of the composition of Claim 46.

#### *Claim Rejections - 35 USC § 112, fourth paragraph*

The fourth paragraph of 35 USC 112 states:

Subject to the following paragraph, a claim in dependent form shall contain a reference to a claim previously set forth and then specify a further limitation of the subject matter claimed. A claim in dependent form shall be construed to incorporate by reference all the limitations of the claim to which it refers. (emphasis added).

Claim 49 is rejected for not providing a further limitation of the subject matter claimed. To wit, Claim 46 requires an oligonucleotide, while Claim 49 requires it to be in single strands, double strands, or complex folding. Considering that triple-stranded is complex folded, that

more than 3 strands would be more complex folding, it would appear that this claim is not further limiting on the claim from which it depends.

***Claim Rejections - 35 USC § 102***

(e) the invention was described in (1) an application for patent, published under section 122(b), by another filed in the United States before the invention by the applicant for patent or (2) a patent granted on an application for patent by another filed in the United States before the invention by the applicant for patent, except that an international application filed under the treaty defined in section 351(a) shall have the effects for purposes of this subsection of an application filed in the United States only if the international application designated the United States and was published under Article 21(2) of such treaty in the English language.

Claim 46 and 48-50 are rejected under 35 U.S.C. 102(e) as being anticipated by U.S.

Patent Application Publication No. 2006/0159737 to Panzer, et al., or, in the alternative, as not being patentable under 35 USC 103(a), to the same reference, as further evidenced by <http://www.rockefeller.edu/labheads/tuschl/sirna.html>.

The applied reference has a common inventor with the instant application. Based upon the earlier effective U.S. filing date of the reference, it constitutes prior art under 35 U.S.C. 102(e). This rejection under 35 U.S.C. 102(e) might be overcome either by a showing under 37 CFR 1.132 that any invention disclosed but not claimed in the reference was derived from the inventor of this application and is thus not the invention “by another,” or by an appropriate showing under 37 CFR 1.131.

With regard to Claims 46 and 58, Panzer teaches a composition of POPC/DOPE/DOTAP/CHOL at a ratio of 30:10:20:40, which meets the required ratios (e.g., Example 5). Moreover, Panzer teaches that the liposomes are utilized for delivering oligonucleotides which may be chemically modified RNAs (e.g., 0068), and may be to effect RNAi (e.g., 0004).

With regard to Claim 48, as evidenced by it is normal to utilize dsRNAs of large enough size to be cleaved by the enzyme Dicer to make siRNAs (<http://www.rockefeller.edu/labheads/tuschl/sirna.html>, which also suggests that at least in mammalian cells the use of chemically modified RNAs).

With regard to Claim 49, the oligonucleotide is double-stranded.

With regard to Claim 50, the oligonucleotides contain an antisense strand.

With regard to Claim 59, the oligonucleotide is an siRNA.

Alternatively, it may be argued that siRNA is listed in the background of the invention, and that therefore, it is not taught.

On the other hand, it is clear from the publication that the purpose of these liposomes is to delivery oligonucleotides (e.g., paragraph 0072), and that siRNA is an oligonucleotide (as evidenced by <http://www.rockefeller.edu/labheads/tuschl/sirna.html>), and hence, the Artisan would have been motivated to make the invention to deliver oligonucleotides to affect RNAi. Moreover, the Artisan would have expected success, as the components are utilized for Art-recognized purposes.

#### *Claim Rejections - 35 USC § 103*

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

(a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negated by the manner in which the invention was made.

Claims 46-50 are rejected under 35 U.S.C. 103(a) as being unpatentable over U.S. Patent Application Publication No. 2006/0159737 to Panzer, et al., as further evidenced by <http://www.rockefeller.edu/labheads/tuschl/sirna.html>.

As shown above, several of the claims are anticipated and/or obvious over Panzer, as evidenced by <http://www.rockefeller.edu/labheads/tuschl/sirna.html>. On the other hand, the use of a liposomal formulation of Claim 47, while taught in Panzer, is taught as an alternative formulation (example 11), and separate liposomes with antisense RNA was applied to also treat colitis in another example (Example 10).

Hence, given the teachings of Panzer, it would have been obvious to make the composition of the claims. The Artisan would have done so to treat colitis, and would have expected success, because both compositions had already been shown to work, and delivery of the nucleic acid could be achieved (i.e., the compositions are utilized for art-recognized purposes).

#### ***Relevant Art***

The closest (other than Applicant's related patent) relevant art is provided by WO 2005/026372 A1 to Heyes, et al., however, such compositions which comprise the various components in these ratios are not liposomes, and the compositions to liposomes are specifically not taught to comprise these complex mixtures of lipids (p. 50).

***Conclusion***

No claim is allowed.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to ROBERT M. KELLY whose telephone number is (571)272-0729. The examiner can normally be reached on M-F, 9:00am-5:00pm.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Joseph Woitach can be reached on (571) 272-0739. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see <http://pair-direct.uspto.gov>. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

/ROBERT M KELLY/  
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